New Drug Update: 2018

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Bio

• Undergraduate: University of North Carolina at Asheville
• Pharmacy: Campbell University
• Residency: Drug Information at Campbell University
• Faculty:
  – Palm Beach Atlantic University
  – Auburn University: 2006 – Present
Objectives

• Discuss the major steps in the new drug approval process
• Name the major new chemical entities approved by the FDA in 2017 and early 2018
• Recognize the major therapeutic aspects of new drugs approved by the FDA in 2017/18 (eg, indications, adverse reactions, drug interactions);
• Identify drugs approved by the FDA in 2017/18 that represent a major therapeutic advancement.
New Drug Approvals

• Approvals By Year
  – 2014: 44
  – 2015: 45
  – 2016: 22
  – 2017: 46
Expedited Approval Categories

• Priority Review
  – Serious conditions
  – Significant improvement over current options

• Accelerated Review
  – Clinical benefit for unmet therapeutic needs

• Fast Track
  – Drugs for unmet therapeutic needs
  – More manufacturer/FDA interaction
FDA Approval Process Changes

- Alzheimer’s
  - Studies can assess biomarkers prior to disease progression
  - “Currently, there is no consensus as to particular biomarkers that would be appropriate to support clinical findings in trials in early AD.”
FDA Approval Process Changes

• Migraine
  – Pain relief and patients “most bothersome symptom”
  – Previously: pain, nausea, photophobia, phonophobia

• Pediatric Epilepsy
  – Adult efficacy data will likely be sufficient
NEW DRUGS 2017-2018
Steglatro (ertugliflozin)

- **Indication**
  - Glycemic control in type 2 diabetes

- **Mechanism**
  - Increases urinary glucose excretion by inhibiting SGLT2

- **Dosing**
  - 5mg starting in the morning
  - 15mg if needed
Steglatro (ertugliflozin)

• Adverse Reactions
  – Urinary tract infections/complications
  – Hypotension
  – Renal function changes

• Drug Interactions
  – Other glycemic control agents
Question 1

• Which “flozin” produces the largest average drop in HgbA1c as monotherapy?

A. Canagliflozin
B. Dapagliflozin
C. Empagliflozin
D. Ertugliflozin
Question 1

• Which “flozin” produces the largest average drop in HgbA1c as monotherapy?

A. Canagliflozin
B. Dapagliflozin
C. Empagliflozin
D. Ertugliflozin
Steglatro (ertugliflozin)

• Clinical Notes

<table>
<thead>
<tr>
<th></th>
<th>Steglatro ertugliflozin</th>
<th>Jardiance empagliflozin</th>
<th>Invokana canagliflozin</th>
<th>Farxiga dapagliflozin</th>
</tr>
</thead>
<tbody>
<tr>
<td>HgbA1c Reduction</td>
<td>~0.75% mono</td>
<td>~0.66% mono</td>
<td>~1.0% mono</td>
<td>~0.52% mono</td>
</tr>
<tr>
<td></td>
<td>~0.8% w/metformin</td>
<td>~0.6% add on</td>
<td>~0.7% add on</td>
<td>~0.6-0.8% w/metformin</td>
</tr>
<tr>
<td>FPG Reduction</td>
<td>~32mg/dL</td>
<td>~25mg/dL</td>
<td>~27-35mg/dL</td>
<td>~25mg/dL</td>
</tr>
</tbody>
</table>
Steglatro (ertugliflozin)

• Clinical Notes
  – Weight loss is noted with the SGLT2 agents
Ozempic (semaglutide)

- **Indication**
  - Glycemic control in type 2 diabetes

- **Mechanism**
  - GLP-1 agonist: delays gastric emptying

- **Dosing**
  - 0.25mg to 1mg subcutaneous injection once per week
Ozempic (semaglutide)

• Adverse Reactions
  – Nausea: 15-20%
  – Vomiting: 9%
  – Diarrhea: up to 8%

• Drug Interactions
  – Potential interactions with delayed gastric emptying
    • None clinically noted (atorvastatin)
Ozempic (semaglutide)

- **Clinical Notes**
  - BBW: thyroid tumors

<table>
<thead>
<tr>
<th></th>
<th>Ozempic semaglutide</th>
<th>Trulicity dulaglutide</th>
<th>Byetta/Bydureon exenatide</th>
<th>Victoza liraglutide</th>
</tr>
</thead>
<tbody>
<tr>
<td>HgbA1c Reduction</td>
<td>~1.4-1.6%</td>
<td>~1.4%</td>
<td>~0.99%/~1.6%</td>
<td>0.8%-1.1%</td>
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<tr>
<td>FPG Reduction</td>
<td>~40mg/dL</td>
<td>~30mg/dL</td>
<td>~25mg/dL</td>
<td>~20mg/dL</td>
</tr>
</tbody>
</table>
Question 2

• Which “glutide” do you see most often in your clinical practice?
Symproic (naldemidine)

• Indication
  – Opioid induced constipation in non-cancer pain

• Mechanism
  – Peripheral acting mu-receptor antagonist

• Dosing
  – 0.2mg tablet once daily
Symproic (naldemidine)

- **Adverse Reactions**
  - Abdominal pain: 11%
  - N/V/D

- **Drug Interactions**
  - CYP 3A
    - Azole antifungals, antivirals,
  - Other opioid antagonists
Symproic (naldemidine)

• Clinical Notes
  – ~50% of patients had at least 3 spontaneous bowel movements (SBM) in the past week
    • ~35% of placebo patients also had SBM
Trulance (plecanatide)

• Indication
  – Chronic idiopathic constipation

• Mechanism
  – Increases chloride and bicarb into the intestinal lumen increasing water

• Dosing
  – 3mg tablet once daily
Trulance (plecanatide)

• Adverse Reactions
  – Diarrhea: 5%

• Drug Interactions
  – None listed
Trulance (plecanatide)

• Clinical Notes
  – Noted to have less diarrhea than Linzess (linaclotide)
    • 5% vs. 16%
  – 1.1 additional spontaneous bowel movements per week
Anti-Infectives

• Does this look infected?
Vabomere
(meropenem/vaborbactam)

• Indication
  – Adults with complicated urinary tract infections

• Mechanism
  – Penem antibiotic
  – Beta-lactamase inhibitor
Vabomere (meropenem/vaborbactam)

- Dosing
  - 4 gms every 8 hours (3 hour infusion) for up to 14 days
  - Dose adjust if CrCl < 50mL/min
    - 2 gms every 8 or 12 hours
    - 1 gm every 12 hours
Vabomere
(meropenem/vaborbactam)

- Adverse Reactions
  - Headache
  - Infusion site reactions
  - Diarrhea

- Drug Interactions
  - Possibly valproic acid
## Vabomere (meropenem/vaborbactam)

### Clinical Notes

<table>
<thead>
<tr>
<th>Event</th>
<th>VABOMERE n/N (%)</th>
<th>Piperacillin/Tazobactam n/N (%)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical cure or improvement AND microbiological eradication at the End of IV Treatment Visit*</td>
<td>183/186 (98.4%)</td>
<td>165/175 (94.3%)</td>
<td>4.1% (0.3%, 8.8%)</td>
</tr>
<tr>
<td>Clinical cure AND microbiological eradication at the Test of Cure visit approximately 7 days after completion of treatment**</td>
<td>124/162 (76.5%)</td>
<td>112/153 (73.2%)</td>
<td>3.3% (-6.2%, 13.0%)</td>
</tr>
</tbody>
</table>

CI = confidence interval; EOIVT = End of Intravenous Treatment; TOC = Test of Cure
Vabomere (meropenem/vaborbactam)

- Clinical Notes
  - Cost of treatment
    - ~$2400 per day
    - Pip/tazo: ~$80 per day
Question 3

• For Health System Pharmacists:
  – What would be the treatment alternatives in your institution for complicated UTIs?
Solosec (secnidazole)

• Indication
  – Bacterial vaginosis

• Mechanism
  – Nitroimidazole antibiotic

• Dosing
  – Single 2gm packet of granules
    • Tested mixing with applesauce, pudding, and yogurt
Solosec (secnidazole)

• Adverse Reactions
  – Vulvo-vaginal candidiasis: ~10%
  – Diarrhea: ~3%
  – Headache: ~3%

• Drug Interactions
  – None listed (specifically excluded oral contraceptives)
Solosec (secnidazole)

• Clinical Notes
  – Clinical response rates at 21-30 days:
    • Solosec: ~60%
    • Placebo: ~20%

• Therapeutic Class
  – Metronidazole
  – Tinidazole
Mavyret
(glecaprevir/pibrentasvir)

• Indication
  – Hepatitis C (genotypes 1-6)

• Mechanism
  – Protease inhibitor
  – NS5A inhibitor

• Dosing
  – 3 tablets once daily for:
    • 8 weeks for treatment naïve
    • 12-16 weeks for patients with previous treatment
    • Don’t use in patients with cirrhosis
Mavyret (glecaprevir/pibrentasvir)

• Clinical Notes
  – Sustained Virallogic Response at 12 weeks:
    • 98% in treatment naïve patients with HCV1
    • 92-94% in treatment experienced patients
  – 8 week cost of treatment: ~$30,000
Vosevi
(sofosbuvir/velpatasvir/voxilaprvir)

- **Indication**
  - Hepatitis C infection
    - Patients who have been treated previously

- **Mechanism**
  - Protease inhibitor
  - NS5A inhibitor

- **Dosing**
  - One tablet daily with food for 12 weeks
Vosevi
(sofosbuvir/velpatasvir/voxilaprevir)

• Clinical Notes
  – Sustained Virallogic Response: 96-100%
  • Comparison Studies
    – Sofosbuvir/velpatasvir: ~85%

  – Cost of treatment: ~$87,000
Movement/Neurological Disorders
Ingrezza (valbenazine)

• Indication
  – Tardive dyskinesia

• Mechanism
  – Unknown: regulation of monoamines

• Dosing
  – 40mg tablet daily for one week
  – 80mg daily (two 40mg tablets)
Ingrezza (valbenazine)

- Adverse Reactions
  - Somnolence: 11%

- Drug Interactions
  - Paraoxetine, fluoxetine
Ingrezza (valbenazine)

• Clinical Notes
  – 84% of patients were currently taking an antipsychotic (14% on first generation or combo)
Figure 4: Percent of Patients with Specified Magnitude of AIMS Total Score Improvement at the End of Week 6

Magnitude of Improvement from Baseline in AIMS Dyskinesia Total Score

Figure is based on ITT: Placebo (N=76), 40mg (N=70), 80mg (N=79).
Ocrevus (ocrelizumab)

• Indication
  – Relapsing remitting MS
  – Primary progressive MS

• Mechanism
  – Inactivates B-lymphocytes: immunosuppressive
Ocrevus (ocrelizumab)

• Dosing
  – At initiation of therapy give first two infusions 2 weeks apart
  – Infusions should follow every 6 months afterwards
  – Pre-medicate for infusion reactions
Ocrevus (ocrelizumab)

• Adverse Reactions
  – Infusion site reactions: ~40%
  – Upper respiratory infections: ~44%

• Drug Interactions
  – Any other immunomodulator
Ocrevus (ocrelizumab)

• Clinical Notes
  – Studies were 96 weeks
  – Percent of patients relapse free
    • Ocrevus: 83%
    • Interferon: 71%
  – Annualized relapse rate
    • Ocrevus: 0.156
    • Interferon: 0.292
Other Agents of Interest

• Symdeko (tezacaftor/ivacaftor)
  – Indication: Cystic Fibrosis

• Biktarvy (combo product)
  – Indication: HIV

• Xepi (ozenoxacin)
  – Indication: Impetigo
Advances in Cancer Treatment

• 12 new agents in 2017
  – Leukemia
  – Breast
  – Lymphoma

• 2 new in 2018
  – Prostate
  – Pancreas/GI tract
Erleda
Question 4 & 5

• Which agents discussed today have been effective in your experience?

• Which agents do you feel represent a therapeutic advancement?
Top $$$$$$$

• Biktarvy: $3.2B
• Ozempic: $1.8B
• Epacadostat: $1.6
• Sublocade/Indivior: $767M
Questions???
What is up with your beard?
Questions???